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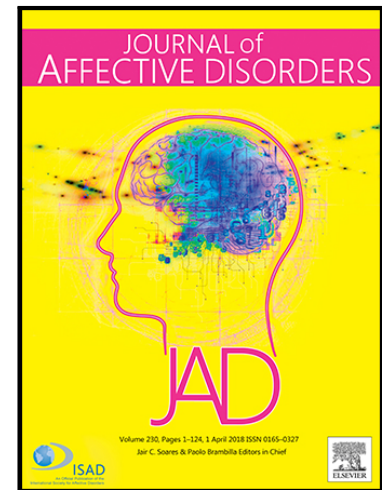
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Highlights

- We examined environmental and genetic determinants of perceived social support
- Reporting longitudinal changes from adolescence to middle adulthood
- Family environment was strongly associated with the initial level of social support
- Rate of change in perceived family support was dependent on *OXTR* genotype

Oxytocin receptor gene (*OXTR*) variant rs1042778 moderates the influence of family environment on changes in perceived social support over time

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Abstract

Background: Lack of social support is an established risk factor across health outcomes, making it important to examine its family environmental and genetic determinants.

Methods: In a 27-year follow-up of the Young Finns Study (N=2341), we examined with a latent growth curve model whether genes involved in the oxytocin signaling pathway—namely, oxytocin receptor gene (OXTR) variants rs1042778, rs2254298, and rs53576—moderate the effect of early-life social experiences on perceived social support across the life span. Mothers reported the emotional warmth and acceptance towards their children at baseline when the participants were from 3 to 18 years old (1980). Perceived family support and support from friends and peripheral sources were assessed in five follow-ups 18 years apart (1989-2007).

Results: Maternal emotional warmth and acceptance predicted the initial level of perceived social support across subscales, while the rate of change in family support was affected by the family environment only if participants carried the T-allele of OXTR rs1042778. This gene-environment interaction was not found for the rate of change in support from friends and peripheral sources and we also did not find associations between latent growth in perceived social support and OXTR variants rs53576 and rs2254298.

Limitations: Selective attrition in perceived social support, maternal emotional warmth and acceptance, gender, and SES. Family environment was assessed by a non-standardized measure.

Conclusions: OXTR rs1042778 polymorphism seems to contribute to changes in perceived family support in that way that some individuals (T-allele carriers)

‘recover’, to some extent, from the effects of early-life social experiences, whereas others (G/G genotype carriers) do not.

Introduction

Humans are highly social animals whose lives are dependent on other humans. A rich literature has demonstrated that social support is a key determinant in human health and well-being (Berkman, Glass, Brissette, & Seeman, 2000; Holt-Lunstad et al., 2015; Uchino, Cacioppo, & Kiecolt-Glaser, 1996; Yang et al., 2016). In addition, social support is especially relevant to mental health as it has been associated with better mental health both directly (Gariépy, Honkaniemi, & Quesnel-Vallée, 2016) and indirectly (Cohen & Wills, 1985). Broadly, social support can be divided into two categories, that is, one characterized by structural aspects (e.g., the size of social networks or frequency of contacts) and the other by emotional or informational aspects (perceptions of availability of support). Although some studies have examined social network changes (i.e., structural social support) across the lifespan (e.g., Wrzus, Hänel, Wagner, & Neyer, 2013), little is known about how perceptions of social support change over different developmental phases (Antonucci et al., 2014; Carstensen et al., 1999). Available evidence on social support perceptions across the lifespan is mostly based on cross-sectional studies (Pavlova, Körner, & Silbereisen, 2015; Prezza & Pacilli, 2002) or is limited to old age (Costa, Zonderman, & McCrae, 1985; Hakulinen et al., 2016; van Tilburg, 1998), yet, these studies have found that family support is rather stable across all ages while support from friends and peripheral sources decrease throughout adulthood. To our knowledge, no longitudinal study has focused on changes in perceived social support from adolescence to middle adulthood. Accordingly, little attention has been paid to family environmental and

genetic determinants of perceived social support across the lifespan (cf. Antonucci, Ajrouch, & Birditt, 2014).

Family environment

Adolescence and adulthood perceptions of social support might reflect internalized representations of the family environment (see, e.g., Herzberg et al., 1999) and, thus, child-rearing practices and the parent-child relationship quality are probably important for how individuals' experience social support in later life. We argue that this is the case because especially the family environment is an origin of social behaviors and close relationships which are reflected in individuals' perceived support across the lifespan.

Most theories agree that emotional warmth between parent and child (i.e., their love and connectedness) is a main component of a beneficial family environment (Clark & Ladd, 2000; Maccoby, 1980; MacDonald, 1992; Schaefer, 1959).

MacDonald (1992), for instance, conceptualizes warmth as a reward system that facilitates cohesive relationships within the family and parents' investment in their children and their emotional bond. Another, yet related, basic characteristic of the family environment is parental acceptance of child's feelings, opinions, and actions (Maccoby, 1980; Schaefer, 1959). Acceptance is a measure of parents' tolerance and responsiveness toward the child. Low levels of acceptance further capture ambivalent child-rearing experiences (Donath, 2015; Shelton & Johnson, 2006), such as, parental perceptions of the child as demanding and requiring a lot of time and attention, and even perceiving the child in some situations as burdensome (Keltikangas-Järvinen, 2002). Thus, emotional warmth and acceptance are markers of the early-life social experience within a family, which reflect variation in normal parenting experienced

by most individuals during their childhood. To our best knowledge, however, the associations between maternal emotional warmth and acceptance and perceived social support have not been studied longitudinally to date.

Genetic background of perceived social support

With regard to specific genetic pathways, the role of oxytocin (OT) signaling is of recent interest in understanding human social behavior and close relationships (Kumsta & Heinrichs, 2013). The neuropeptide OT has been held responsible for regulating social cognition (Peltola et al., 2014; Skuse et al., 2014; Zink & Meyer-Lindenberg, 2012) as well as various social and affective traits and states (Ebstein, Knafo, Mankuta, Chew, & Lai, 2012; Olff et al., 2013). Perceived social support appears to have a biological makeup (i.e., is partly heritable) (Kessler, Kendler, Heath, Neale, & Eaves, 1992) and genes involved in OT signaling might contribute to inter-individual differences in perceived social support. Here, we focus on the most common type of genetic variation among individuals: single nucleotide polymorphisms (SNPs). SNPs represent naturally occurring variations in a single DNA building block. For example, an SNP may replace the nucleotide Guanine (G) with the nucleotide Adenine (A) or Thymine (T) in a certain stretch of DNA. These genetic differences might be associated with complex traits, such as perceived social support and might also modulate an individual's susceptibility to environmental influences (U.S. National Library of Medicine, 2017).

So far, three studies have investigated the relationship between oxytocin receptor gene (*OXTR*) variant rs53576 and various sources of social support, such as, experimental manipulated presence versus absence of a friend (Chen et al., 2011), the level of perceived unsupportive social interactions with parents and peers (McInnis,

McQuaid, Matheson, & Anisman, 2015), or the self-rated quality of seven aspects of support across relationships with family and nonfamily members (Hostinar, Cicchetti, & Rogosch, 2014). None of these studies, however, have found direct associations between *OXTR* rs53576 and perceived social support.

Gene-environment (GxE) interactions

The fact that previous research did not find direct effects of oxytocin pathway genes in social support perceptions might be explained by GxE interaction. It is possible that the associations between the family environment and perceived social support might be different in different *OXTR* genotype carriers, which makes it important to examine GxE interactions in perceived social support across adolescence and adulthood.

Generally, research on GxE interactions has to differentiate between at least three complementary perspectives: The *diathesis-stress perspective* is guided by the theoretical assumption that some individuals are more vulnerable than others to adverse environments for genetic (or temperamental) reasons (Caspi et al., 2002; Rutter, Moffitt, & Caspi, 2006). A logical complement to this concept was recently coined *vantage sensitivity* (Pluess & Belsky, 2013), claiming that there are inter-individual differences in the response to positive environmental influences as a function of opportunity characteristics. The *differential susceptibility hypothesis*, finally, states that some individuals are more susceptible than others to all environmental effects irrespective of their nature (Belsky & Pluess, 2009). Those individuals who carry certain “plasticity-alleles” are thus not just vulnerable to environmental risks (as the *diathesis-stress perspective* suggests) but also sensitive to effects of neutral or beneficial environments (as the concept of *vantage sensitivity*

implies). What all three perspectives have in common, is that for other individuals the same environmental influences might have only a weak effect, if any. Moreover, genes might not only modulate the effect an environmental determinant has on initial differences in a social phenotype but also influence whether these differences become more pronounced, decrease, or even disappear as individuals grow older.

Therefore, common polymorphisms in OT pathway genes might moderate how salient the family environment is in perceptions of social support (Kumsta & Heinrichs, 2013). For instance, maltreated adolescents carrying the G/G genotype in *OXTR* variant rs53576 are shown to have lower perceived social support as compared to carriers of the A-allele, who are not affected by this environmental influence (Hostinar et al., 2014).

Three candidate genes appear most promising for examining GxE interactions in perceived social support: The first two SNPs, rs53576 and rs2254298 (both G to A), have been targeted at in recent meta-analytical (Bakermans-Kranenburg & van Ijzendoorn, 2014; Li et al., 2015) and theoretical reviews (e.g., Brune, 2012). The third SNP, rs1042778 (G to T), is an early-discovered candidate gene (Israel et al., 2009), which has repeatedly been mentioned in literature on *OXTR*-social behavior linkages. For all three SNPs functional linkages to either alterations of oxytocinergic brain regions as responses to social cues (Inoue et al., 2010; Tost et al., 2010), OT plasma levels (Feldman et al., 2012), and/or DNA CpG methylation (Smearman et al., 2016) have been reported.

The current study

As early-life social experiences can lay a foundation for human development across the lifespan, the family environment might continue to influence individuals'

perceptions of social support during adolescence and adulthood. However, this might be the case only if the child (and later adult) carries certain genotypes in the *OXTR* that make him/her more *susceptible* to environmental influences. The current study, therefore, examines if candidate genes in the oxytocin receptor moderate the influence of maternal emotional warmth and acceptance on perceptions of social support. Furthermore, we report the changes in social support from adolescence to middle adulthood, which has not been longitudinally investigated previously. This makes it possible to study conditional effects of the *OXTR* and the family environment on perceived social support over time. The following hypotheses will be tested by a sequence of latent growth curve models:

Hypothesis 1: Variation in maternal emotional warmth and acceptance has a direct effect on the initial levels and the rate of change of perceived social support. Thus, individuals raised in a more beneficial family environment are expected to report higher levels of social support later in life.

Hypothesis 2: *OXTR* genotypes have a direct effect on the development of perceived social support. We expect, therefore, that individuals with a stronger genetic predisposition for social vulnerability will report comparatively lower social support levels.

Hypothesis 3: The interaction between *OXTR* genotypes and the family environment is partially responsible for high or low levels of perceived social support. This final hypothesis assumes that individuals are differential susceptible to environmental influences for genetic reason.

Materials and methods

Setting

The current study uses data from the Young Finns Study (YFS) (Åkerblom et al., 1991; Raitakari et al., 2008), which is a longitudinal cohort study that was designed to examine determinants of cardiovascular risk in a representative Finnish sample. YFS was started in 1980 (T0) when the participants were children and adolescents. The last follow-up has been conducted in 2011/12 in participants' middle adulthood. The procedure of the YFS has been described in more detail previously (Raitakari et al., 2008). In the current study data from years 1980 (baseline), 1983, 1989, 1992, 1997, 2001, and 2007 were used. The study was conducted in compliance with the Helsinki Declaration. The study was approved by local ethics committees and written informed consent was obtained either from the participants themselves or their parents depending on the participant's age.

Participants

In total 3596 participants (aged 3, 6, 9, 12, 15, or 18 years at baseline) composed the initial sample. The participants were evenly distributed across the six age groups (15.1% - 17.5%). We excluded participants if they had missing information on the family environment (Figure 1) and used data from those 2341 participants (55% female) who answered the social support questions at least once and who agreed to be genotyped.

Insert Figure 1 about here

Measures

Perceived social support

Functional support was assessed with the Multidimensional Scale of Perceived Social Support (MSPSS), a questionnaire presented by Zimet and colleagues (Blumenthal et al., 1987; Zimet, Powell, Farley, Werkman, & Berkoff, 1990). The scale measures perceived social support in three dimensions: family, friends, and a significant other. Perceived social support was assessed in 1989 (T1, when the participants were 12, 15, 18, 21, 24, and 27 years old), in 1992 (T2), in 1997 (T3), in 2001 (T4), and in 2007 (T5). Each subscale includes four items, such as, “There is a special person who is around when I am in need.” that were rated on a 5-point Likert scale (1 = strongly disagree, 5 = strongly agree). The MSPSS has good psychometric properties, and its subscales show discriminant validity (Canty-Mitchell & Zimet, 2000; Clara, Cox, Enns, Murray, & Torgrudc, 2003). For the purpose of the current study, the friends and significant other support items were combined into a single measure because both dimensions measure perceived social support provided by friends and peripheral sources. Cronbach’s alphas were high ranging from 0.90 (at T2 for family support) to 0.97 (at T5 for support from friends and peripheral sources), with higher scores indicating higher perceptions of social support.

Family environment

The family environment (i.e., maternal emotional warmth and acceptance) was assessed with items derived from the Operation Family Study (Makkonen et al., 1981; Savelieva et al., 2016). Maternal emotional warmth was assessed with four items: “I enjoy spending time with my child”; “I am important to my child”; “My child is important to me”; and “My child enables me to self-actualize myself.” The maternal

emotional warmth scale ranges from 1 (*never or almost never*) to 5 (always or almost always). Mothers' acceptance of the child was measured with three items: "In difficult situations, the child is a burden"; "I often become irritated with my child"; and "My child takes too much of my time." The maternal acceptance scale ranges from 1 (*always or almost always*) to 5 (*never or almost never*). The maternal acceptance items were reversed so that for both mother-rated components higher scores indicate a more beneficial family environment. We combined these two scales to a broad measure of the family environment, which had a Cronbach's alpha of 0.70. The family environment was mainly reported in 1980, but in few cases (N=37) missing values were filled with answers provided in 1983 on the same questions. Finally, the measure was cubic root transformed and standardized within the six age groups to eliminate the potential differences in the mother-reports due to their child's age.

Parental socioeconomic status.

Socioeconomic status was assessed based on three variables which were fielded at baseline. The average years the mother and the father spend in the educational system were first standardized and then summed to parental education. The annual income of the family (measured on an eight-point scale) was standardized. Finally, parental education and family income were summed to form a composite measure of parental socio-economic status. As the participants were randomly chosen from the population register to produce a representative sample, 0 on the final socioeconomic status variable refers to the average adult Finn with children at baseline. This covariate, which has been used in previous YFS studies (e.g., Hakulinen et al, 2013), was included because individuals whose socioeconomic status was low have been found to

show a different reaction to social support in stressful circumstances, as compared to those with high levels (John-Henderson, Stellar, Mendoza-Denton, & Francis, 2015).

Genotyping.

The genome-wide analyses for the participants of the YFS were performed in 2009 (for details see Smith et al., 2010). SNPs rs1042778 and rs53576 were directly genotyped using an Illumina 670k genotyping array. Imputation of rs2254298 was done using the IMPUTE2 software (Howie et al., 2009) and the 1000 Genomes Project March 2012 haplotypes as a reference, resulting in an excellent imputation quality (info ~ 0.99). Rs1042778, rs2254298, and rs53576 are located in chromosome 3, on position 8752859, 8760542, and 8762685, respectively.

Statistical analysis

We used multiple indicators Latent Growth Curve Modeling (LGCM) (Bishop, Geiser, & Cole, 2015) to examine inter-individual variability in the initial levels, i.e., intercept, of perceived social support and the rate of change, i.e., slope, in participants' perception of social support when growing 18 years older. A good fit of the data to the model is indicated by a CFI value ≥ 0.95 and an RMSEA value ≤ 0.05 (Hu & Bentler, 1999). All calculations were conducted with the statistical programming software "R" (version 3.1.2 (2014-10-31)).

We ran a sequence of four LGCMs. Model 1 describes a developmental model and controlled for the covariates gender, age, and socioeconomic status by regressing them on the latent intercept and the latent slope of the perceived social support subscales. As age was centered at T1, the intercept should be interpreted as the expected level of perceived social support for an individual at the sample mean age (19.5 years) at this wave (cf. Mehta & West, 2000). The model also includes a control

for a period effect observed for perceived social support at T1 (potentially related to the economic recession of the early 1990s in Finland), which negatively affected participants' perceived social support across all ages. The next two models examine the direct effects of family environment (Model 2; Hypothesis 1: direct effect of maternal warmth and acceptance) and the three candidate genes in the oxytocin receptor (Model 3; Hypothesis 2: direct effect of *OXTR*) on social support growth curves. In the final Model 4, the cross-product term for the genetic moderation of the family environment on perceived social support was added to test the differential susceptibility hypothesis (Hypothesis 3: GxE interaction effects). Note that each genotype and each respective interaction were analyzed separately. The continuous variables, that is, age and maternal emotional warmth and acceptance, were standardized before entering into the models and all analyses were conducted with full information maximum likelihood (FIML) estimator to account for missing data (Allison, 2012). Finally, we illustrated how the observed GxE interaction effects influence the changes in perceived social support over time.

Descriptive statistics

Descriptive statistics for the analytic sample are presented in Table 1. Included participants were more likely to report higher scores on perceived family support (mean difference (ΔM) = 0.14, $p < .01$ (T4)) and support from friends and peripheral sources (ΔM s = 0.10, $p = .02$ (T1); 0.09, $p = .03$ (T2); 0.14, $p < .01$ (T4)) than excluded participants. Included participants were also slightly more likely to be female (difference 11 percent points; $X^2 = 39.99$), raised in a household with higher socioeconomic status ($\Delta M = 0.08$, $p < .01$), and their mothers reported somewhat higher emotional warmth and acceptance ($\Delta M = 0.07$, $p < .01$) than those who were excluded

from the current study. The frequencies of the three *OXTR* SNPs rs1042778 ($p=.99$), rs2254298 ($p=.31$), and rs53576 ($p=.09$) did not deviate from the Hardy-Weinberg equilibrium, yet the A-allele of rs2254298 was quite uncommon, and therefore carriers of A/A and G/A genotypes were combined in the subsequent analyses. For the two other *OXTR* SNPs, an additive genetic model was applied (SNPs are coded 0, 1, 2; counting the copies of the G-allele). By doing so, we assume that G/G genotype carriers have a linearly stronger genetic predisposition for social vulnerability/plasticity than carriers of one or two minor alleles of these *OXTR* SNPs, as the A- and T-alleles have repeatedly been shown to be associated with a social deficits and impairments (Bakermans-Kranenburg & van Ijzendoorn, 2014; Feldman et al., 2012; Hostinar et al., 2014; Inoue et al., 2010; Li et al., 2015; Smearman et al., 2016; Tost et al., 2010).

Insert Table 1 about here

Results

Multiple indicator latent growth curve models of perceived social support

For the two perceived social support scales, the global fit indices indicated that a linear trajectory describes the data well. RMSEA ($<.05$) and CFI suggested a good fit ($\geq .97$) for family support (Table 2) across models. For support from friends and peripheral sources RMSEA ($\leq .06$) suggested a good fit and CFI an acceptable fit ($\geq .92$; Table 3).

Insert Tables 2-3 about here

In the initial developmental models (Model 1), the point estimates of the latent slope indicated that participants in average increased in family support (.15) but decreased in support from friends and peripheral sources (-.13).

The initial level (i.e., the latent intercept) of perceived social support (across scales) was higher in women than in men and in those participants with high socioeconomic status as compared to low socioeconomic status participants. The rate of change (i.e., the latent slope) of perceived support from friends and peripheral sources, however, decreased significantly faster for female participants. The older the participants were at baseline, the higher was their initial level of perceived support provided by friends and peripheral sources. The negative regression coefficient of age on latent slopes indicated that perceived family support increased somewhat slower and perceived support from friends and peripheral support decreased somewhat faster for those participants who entered the study at a younger age. The inclusion of a period effect for the 1998 wave, as expected, affected the intercept of perceived family support and the slope of perceived support from friends and peripheral sources significantly.

Family environment, which combines mothers' ratings of emotional warmth and acceptance, was strongly associated with the initial level of both perceived family support and perceived friends and more peripheral support (Model 2). There was, however, no direct effect of the family environment on the rate of change in perceived social support.

We did not observe any significant direct effects of the three *OXTR* candidate genes on latent growth in social support (Model 3).

In Model 4 interaction was found between the number of T-alleles of rs1042778 and variation in maternal emotional warmth and acceptance on the rate of

change of perceived family support, which remained significant when Bonferroni correction was conducted (p-value of $<.017$). For rs1042778 G/G genotype carriers, change in perceived family support over time was not dependent on family environment. For carriers of one or two copies of the T-allele of rs1042778, on the contrary, change in perceived family support over time was associated with the family environment. When maternal emotional warmth and acceptance were low, rs1042778 T-allele carriers increased at a faster rate in perceived family support, while the pattern was reversed if these participants were raised by mothers that described the family environment as beneficial.

Insert Figure 2 about here

The sample was further split into three groups according to high, average, and low levels of maternal emotional warmth and acceptance. We estimated for these groups their latent means to capture the change in family support across waves (T1-T5). Figure 2 illustrates the consequences of this GxE interaction by comparing rs1042778 T/T genotype, G/T genotype, and G/G genotype carriers. The figure shows that rs1042778 G/G genotype carriers who were raised with high maternal emotional warmth and acceptance reported, across the lifespan, higher levels of perceived family support than those who grew up with low levels. G/T genotype carriers of rs1042778 also started at a level of perceived family support that was dependent on whether they were raised in a beneficial family environment or not. However, these differences decreased steadily as these T-allele carriers grew older, until, at T5 (when participants were from 30 to 45 years old), no visible differences remained. T/T genotype carriers

of rs1042778 were in the long run, compared to G/G genotype carriers, also less affected by the maternal emotional warmth and acceptance during childhood.

Discussion

Current study results indicate that the family environment may be directly associated with variation in perceived social support but not with its development over time. *OXTR* genotype was not directly associated with perceived social support, but we found a GxE interaction for the family support domain showing that the influence of family environment does not last for some individuals depending on their rs1042778 genotype. These GxE interactions were not observed for rs2254298 and rs53576 or support from friends and peripheral sources.

Presented results are in line with the differential susceptibility hypothesis (Belsky & Pluess, 2009), stating that some individuals are genetically more susceptible to environmental influences irrespective of their nature, while for other individuals, the same environmental determinants might have no effect. Our findings indicate that, although there are initial differences in perceived social support, they disappear entirely for carriers of the G/T genotype of rs1042778 and weaken for T/T genotype carriers, while the initial differences in perceived family support seem to persist over time for individuals with the G/G genotype. Please note that, in our main analyses, we have followed an additive inheritance model, which assumes linear effects. Overall, the findings suggest that rs1042778 T-allele carriers are likely to ‘recover’ from the effects of low maternal emotional warmth and acceptance whereas G/G genotype carriers do not show such a pattern. In them, the effect of the family environment on social support seems to continue throughout the lifespan, which indicates that early-life social experience “programs” how G/G genotype carriers perceive social support later in life. This has importance for potential preventions.

Similar “programming” has been found for instance for environmental risk on children’s attachment (Bakermans-Kranenburg & van Ijzendoorn, 2007). Current findings should be replicated to verify whether the genetic moderation of *OXTR* rs1042778 is conditional to age, as suggested by our results.

This observation suggests that, for some individuals, later life outcomes have their origin in childhood experiences, while others are less influenced by their family history. However, this lower susceptibility seems to come at a cost: it appears that for these individuals, a beneficial family environment does not continue to have a positive influence on later social support. Current results further add to the existing literature on GxE interaction in social support (Hostinar et al., 2014), which has found that *OXTR* variant rs53576 moderated the influence of adverse environmental influences. At the same time, they are at odds with these previous works as our environmental determinant did not interact with rs53576 polymorphism. Brune (2012) has further argued theoretically that *OXTR* polymorphism rs2254298 might confer differential susceptibility and not merely vulnerability for psychopathological characteristics of individuals. *OXTR* rs1042778, to our best knowledge, has previously not been proposed as a susceptibility gene.

That we did not find a direct effect of *OXTR* rs1042778, rs2254298, and rs53576 is in line with earlier research on social support (Chen et al., 2011; Hostinar et al., 2014; McInnis et al., 2015). However, earlier studies have found polymorphisms in our three candidate genes to be related to differences in social phenotypes that are linked to social support, such as, loneliness (Lucht et al., 2009), trust behavior (Krueger et al., 2012) and, most importantly, emotional support seeking (Kim et al., 2010). Our GxE findings might explain why literature on the role of *OXTR* in human social behavior is inconclusive because rs1042778 polymorphisms

moderated the influence of an early-life social experience on perceived social support instead of having a direct genetic association. Thus, it is likely that the associations between social support and other social environments may also be different in different *OXTR* genotype carriers.

The family environment had a direct effect on the initial level of both perceived social support domains. It may be that children form internal representations of maternal emotional warmth and acceptance, which in turn continue to influence perceptions of both family support and support from friends and more peripheral sources. Prior to this study family environmental determinants of perceived social support were essentially unknown (for an exception, see Herzberg et al., 1999), even though child-rearing practices and maternal warmth and acceptance have repeatedly been shown to affect the development of personality (e.g., Maccoby, 1980; Hakulinen et al., 2013) and the later adjustment of the offspring (e.g., Gluschkoff et al., 2017).

We found in longitudinal data that family support increased and support from friends and peripheral sources decreased over the observed age span from 12 (age of the youngest age cohort at T1) to 45 (age of the oldest age cohort at T5) years. That perceived social support provided by friends and more peripheral sources decrease from adolescence to middle adulthood is in line with leading developmental models on social support (Antonucci, Ajrouch, & Birditt, 2014; Carstensen, Isaacowitz, & Charles, 1999) and matches available cross-sectional evidence (Pavlova, Körner, & Silbereisen, 2015; Prezza & Pacilli, 2002). Our findings that perceived family support actually increases from adolescence to middle adulthood rather than being stable is somewhat surprising (see Wrzus et al., 2013). Normative, age-related life events might explain this finding, as middle adulthood is the period in which participants

start to have children of their own, which in turn might increase the contact frequency to their parents (Bhattacharya et al., 2016).

Limitations and Strengths

The current study has some limitations. The study results were affected by attrition, which was somewhat selective for perceived social support and maternal environmental warmth and acceptance, but also gender and socio-economic status. Family environment was assessed by a non-standardized measure. The mother-reports of the emotional warmth and acceptance might have rather different meanings with children aged 18 years compared to aged 3 years, we, thus, standardized the environmental determinant within age group to overcome this limitation. However, we did not analyze the birth cohorts separately, as suggested by Mehta and West (2000), because that would have reduced the statistical power to detect genetic moderation. Further, we discovered a period effect for the first assessment of social support which altered participants' answers across all ages and consequently had to be controlled for statistically. It was also not possible with our data to control for additional intervening variables, such as life events that might explain some of the observed changes in social support over time (e.g., marriage, divorce, or having children). Last, although around fifth of the participants has reported using antidepressants at some point of their life (Hintsala et al., 2016), most participants were healthy, and thus a generalization of current results to clinical settings is limited.

The strengths of the current study include our longitudinal population-based data, analyzing change in the dependent variable over 18 years until the middle adulthood, and using four repeated measurements with 2341 participants based on a well-established scale that assesses functional social support in two meaningful

relationship domains. Most previous GxE interaction studies have not had enough statistical power to detect robust associations (Duncan & Keller, 2011). Further, the reported associations are not confounded by common method variance as the family environment was reported by mothers and adolescence, and adulthood social support was reported the participants. Finally, we examined the effect of three most promising polymorphisms in genes involved in the oxytocin signaling pathway instead of selecting a single SNP.

Conclusions

The current study showed that an *OXTR* candidate gene (*rs1042778*) moderates the influence of the family environment (i.e., maternal emotional warmth and acceptance) on perceived social support later in life. The observed GxE interaction has important theoretical implications. Participants who carry certain genes in the oxytocin signaling pathway—namely, the G/G genotype of *OXTR* variant *rs1042778*, profited from the more beneficial family environment during childhood, but the maternal emotional warmth and acceptance did not have an effect on changes in their perceptions of family support over time. Initial family support levels of carriers of the T-allele of *rs1042778* were as well affected by their family environment, yet, the effect of this environmental determinant faded so that, in the long run, these individuals were less susceptible to the influence of maternal emotional warmth and acceptance than others. Taken together, our findings can be interpreted in a way that, with age, some individuals might become less affected by family environmental determinants of perceived social support for genetic reason, whereas others (G/G carriers) are “programmed” by early-life social experiences to perceive social support in certain way later in life.

Our findings also have potential practical implications. If replicated (see, e.g.,

Keers & Pluess, 2017), current findings suggest that intervention or prevention programs designed to improve childhood environment may lead to higher social support over the life course, particularly among those with genetic sensitivity.

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Table 1. Demographic Statistics of the Study Variables

<i>Variable</i>	<i>No.of Cases</i>	<i>Mean(%)</i>	<i>SD</i>
Men	1058	(45)	
Women	1283	(55)	
Age in 1989	2341	19.45	5.02
Socioeconomic status	2322	0.02	0.66
Family environment (raw)	2341	4.22	0.47
rs1042778 T/T	352	(15)	
G/T	1112	(48)	
G/G	877	(37)	
rs2254298 A-allele	380	(16)	
G/G	1961	(84)	
rs53576 A/A	446	(19)	
A/G	1105	(47)	
G/G	790	(34)	
Perceived family support (T1)	1981	3.93	0.92
(T2)	1779	4.11	0.87
(T3)	1595	4.15	0.90
(T4)	1722	4.24	0.86
(T5)	1712	4.19	0.88
Perceived support from friends and peripheral sources (T1)	1986	3.91	0.93
(T2)	1779	4.21	0.85
(T3)	1595	4.31	0.81
(T4)	1728	4.22	0.88
(T5)	1712	4.19	0.90

Note. Perceived social support subscales were calculated as a mean of four / eight items. Family environment was calculated as a mean of seven items assessing maternal emotional warmth and acceptance. Socioeconomic status, measured with

parental education and income, was standardized within the initial sample (0 representing the average adult Finn at baseline).

Table 2. Perceived Family Support

<i>Model</i>		<i>Intercept</i>	<i>(SE)</i>	<i>p</i>	<i>Slope</i>	<i>(SE)</i>	<i>p</i>
Model 1	Developmental model						
	Latent means	3.962	0.068	<0.001	0.152	0.050	0.002
	Gender (male=1; female=0)	-0.125	0.038	0.001	-0.017	0.028	0.559
	Age	0.033	0.019	0.077	-0.071	0.014	<0.001
	Socioeconomic status	0.051	0.022	0.018	0.027	0.016	0.089
	Period effect for 1989 (T1=1; T2-T5=0)	0.180	0.068	0.008	-0.022	0.049	0.654
Model 2	Adding direct effect of family environment						
	Emotional warmth and acceptance (EWA)	0.116	0.018	<0.001	-0.006	0.014	0.655
Model 3	Adding direct effects of <i>OXTR</i>						
	rs1042778 (G to T)	-0.010	0.027	0.712	-0.006	0.020	0.780
	rs2254298 (G/G genotype=1; A-allele=0)	-0.058	0.050	0.246	0.055	0.038	0.129
	rs53576 (G to A)	-0.047	0.026	0.072	0.013	0.019	0.503
Model 4	Adding GxE interactions						
	EWA*rs1042778	-0.027	0.027	0.306	0.055	0.020	0.006
	EWA*rs2254298	-0.042	0.048	0.381	0.043	0.036	0.223
	EWA*rs53576	0.033	0.024	0.165	-0.021	0.018	0.240

Table 3. Perceived support from friends and peripheral sources

<i>Model</i>	<i>Intercept</i>	<i>(SE)</i>	<i>p</i>	<i>Slope</i>	<i>(SE)</i>	<i>p</i>
Model 1 Developmental model						
Latent means	4.616	0.064	<0.001	-0.134	0.049	0.006
Gender (male=1; female=0)	-0.639	0.035	<0.001	0.090	0.028	0.001
Age	0.098	0.017	<0.001	-0.124	0.014	<0.001
Socioeconomic status	0.096	0.020	<0.001	-0.022	0.016	0.160
Period effect for 1989 (T1=1; T2-T5=0)	-0.023	0.063	0.720	0.120	0.048	0.013
Model 2 Adding direct effect of family environment						
Emotional warmth and acceptance (EWA)	0.053	0.017	0.002	-0.009	0.013	0.487
Model 3 Adding direct effects of <i>OXTR</i>						
rs1042778 (G to T)	0.017	0.025	0.503	-0.015	0.020	0.438
rs2254298 (G/G genotype=1; A-allele=0)	-0.011	0.047	0.807	0.002	0.037	0.961
rs53576 (G to A)	-0.028	0.024	0.254	0.011	0.019	0.558
Model 4 Adding GxE interactions						
EWA*rs1042778	0.006	0.025	0.818	0.026	0.020	0.183
EWA*rs2254298	-0.030	0.043	0.484	0.015	0.034	0.655
EWA*rs53576	0.022	0.022	0.334	-0.010	0.018	0.561

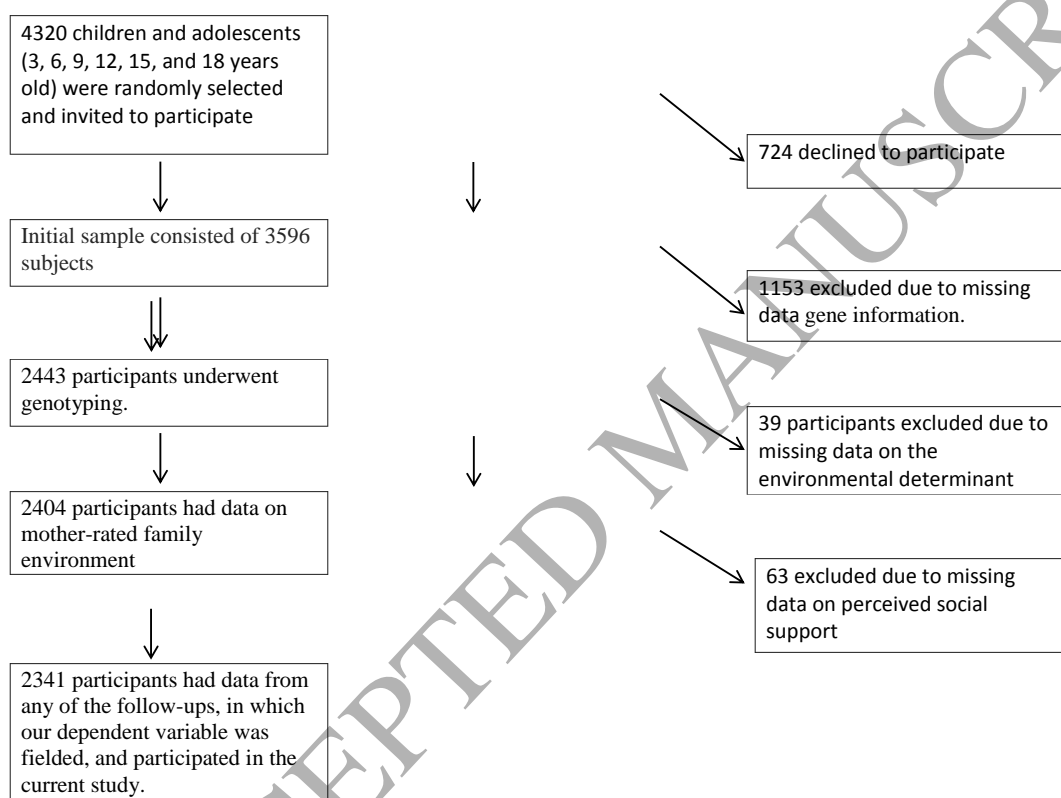
Figure Captions

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Figure 1. Population diagram

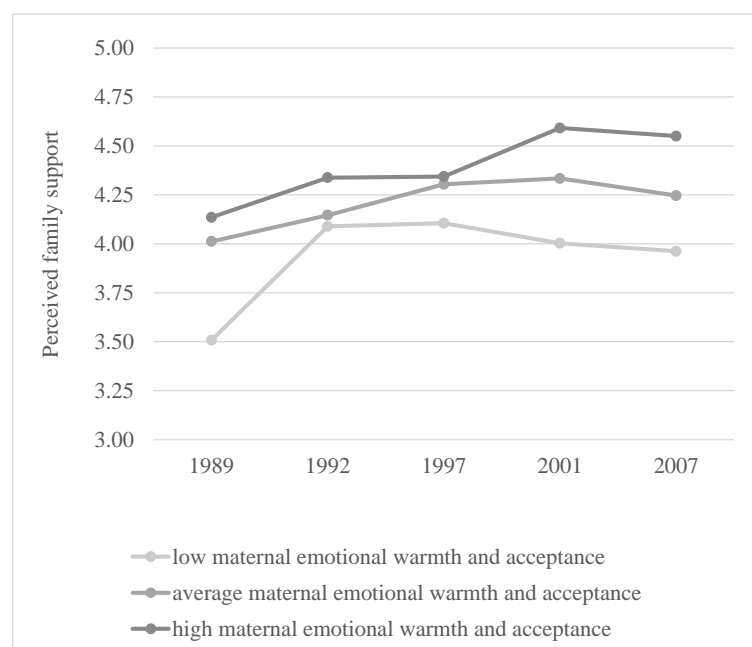
Figure 2. The effect of high and low maternal emotional warmth and acceptance during childhood on the latent means of perceived family support across five YFS waves; split by *OXTR* rs1042778 G/G genotype (a), G/T genotype (b), and T/T (c) genotype carriers. Each genotype and each interaction were analyzed separately.

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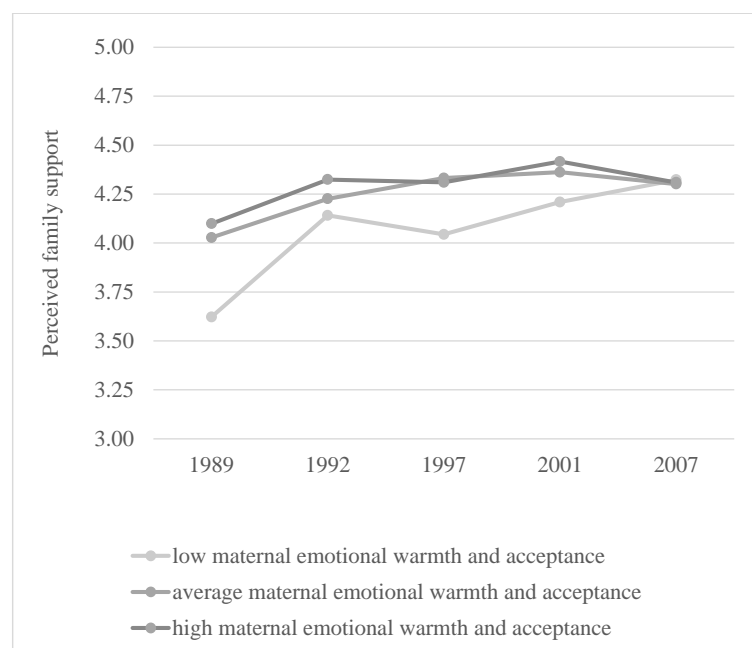
Figure 1.

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Figure 2a) *OXTR* rs1042778 G/G genotype carriers

b) *OXTR* rs1042778 G/T genotype carriers



c) *OXTR* rs1042778 T/T genotype carriers